



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Skin manifestations associated with the new coronavirus SARS-CoV-2 disease*

Manifestaciones cutáneas asociadas a la enfermedad por el nuevo coronavirus SARS-CoV-2

Dear Editor,

The disease caused by the novel coronavirus SARS-CoV-2 (COVID-19) usually presents with respiratory symptoms, but clinical manifestations have been described in other organs, such as the skin. Below we describe the case of a patient with skin symptoms that developed during the recovery period from a coronavirus SARS-CoV-2 pneumonia.

We present the case of a 51-year-old man with no relevant medical history who came to the emergency department due to a dry cough and dyspnea on moderate exertion, for the past 7 days. On physical examination, the patient was eupneic, afebrile, and lung auscultation was normal. The chest X-ray revealed peripheral and bilateral pulmonary opacities, predominantly in the lower lobes, which, in the epidemiological context in Spain in March 2020, was compatible with COVID-19. The polymerase chain reaction (PCR) test for the coronavirus SARS-CoV-2 was positive. The treatment prescribed was hydroxychloroquine for 5 days and lopinavir/ritonavir for 10 days. He remained in hospital for 15 days until clinical improvement was seen, and the PCR result for the coronavirus SARS-CoV-2 was negative. Two days after discharge, an erythematous maculopapular rash with islands of healthy, slightly pruritic skin suddenly presented on his trunk. The prescription given was topical betamethasone dipropionate and 20 mg of oral bilastine, but after 24 h the lesions had spread to the cervical region, face and proximal region of the arms, so 30 mg of prednisone was added orally. The clinical response was favorable, with disappearance of the lesions in a few days.

The novel coronavirus SARS-CoV-2 disease (COVID-19) was first described in Wuhan (China) in December 2019, and is characterized by the appearance of respiratory symptoms, such as fever, dry cough, dyspnea, rhinorrhoea, anosmia and ageusia. The spectrum of respiratory involvement ranges from an upper respiratory tract cold, which can go unnoticed, to severe pneumonia or severe acute respiratory syndrome due to coronavirus 2 (SARS-CoV-2).¹ Although less frequently, dermatological manifestations associated with COVID-19 have been described. In a sample of 88 cases, Recalcati found 18 patients with cutaneous manifestations, including 14 cases of erythematous rash, 3 with widespread urticaria, and a chickenpox-like rash. In most of the patients, cutaneous symptoms appeared after hospital discharge, as in our case, and were

not associated with a greater severity of COVID-19. The lesions mainly affected the trunk, were asymptomatic or slightly pruritic and disappeared in a few days.² These cutaneous symptoms are not specific to COVID-19, but rather they are characteristic of those that occur in other common viral respiratory infections. For example, a case of COVID-19 has been described that was initially confused with dengue due to the similarity of the cutaneous symptoms.³

Other dermatological manifestations to consider are those due to the secondary effects of certain drugs used in the treatment of COVID-19. In particular, consideration should be given to the possible adverse effects to the skin of hydroxychloroquine, such as skin hyperpigmentation, pruritus, xerosis cutis, alopecia, urticaria, morbilliform or maculopapular eruptions, and exfoliative dermatitis.⁴ Azithromycin can also cause skin rashes, pruritus, or Stevens-Johnson syndrome. The most common adverse effects of the lopinavir and ritonavir combination include maculopapular rashes, pruritus, eczema and seborrheic dermatitis.

Other more serious cutaneous lesions have been described, caused by microthrombosis related to endothelial injury and vascular disorders produced in COVID-19. These are sudden-onset ischemic lesions characterized by cyanosis, blistering, and dry gangrene of the fingers and toes.⁵

In conclusion, although it seems highly probable that COVID-19 produces skin disorders, more studies are necessary to know all its forms of presentation and confirm its causal relationship.

Patient consent was obtained, and the working site protocols for the treatment of patient information were followed.

Funding

None.

Conflict of interests

None.

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323:1061–9. <http://dx.doi.org/10.1001/jama.2020.1585>.
2. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol*. 2020. <http://dx.doi.org/10.1111/jdv.16387> [Epub ahead of print].
3. Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. *J Am Acad Dermatol*. 2020. <http://dx.doi.org/10.1016/j.jaad.2020.03.036> [Epub ahead of print].
4. Fernandez AP. Updated recommendations on the use of hydroxychloroquine in dermatologic practice. *J Am Acad Dermatol*. 2017;76:1176–82. <http://dx.doi.org/10.1016/j.jaad.2017.01.012>.
5. Zhang Y, Cao W, Xiao M, Li YJ, Yang Y, Zhao J, et al. Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and acro-ischemia. *Zhonghua Xue Ye Xue Za Zhi*. 2020.

* Please cite this article as: Redondo-Sendino Á, González Sánchez IC, de Victoria Fernández B. Manifestaciones cutáneas asociadas a la enfermedad por el nuevo coronavirus SARS-CoV-2. *Med Clin (Barc)*. 2020;155:414–415.

<http://dx.doi.org/10.3760/cma.jissn.0253-2727.2020.0006> [Epub ahead of print].

Áurea Redondo-Sendino*, Isabel Cristina González Sánchez, Beatriz de Victoria Fernández

Medicina de Familia, Centro de Salud Canillejas, Madrid, Spain

* Corresponding author.
E-mail address: aurearedondo@hotmail.com
(Á. Redondo-Sendino).

2387-0206/ © 2020 Elsevier España, S.L.U. All rights reserved.

Free-floating right heart thrombus with pulmonary embolism in SARS-CoV-2 patient



Trombo intracardiaco con tromboembolia pulmonar en paciente con SARS-CoV-2

Dear Editor,

Infection with SARS-CoV-2 generates alterations in coagulation factors, mainly elevation of D-dimer values. These coagulation disorders jointly with activation of inflammatory factors trigger thrombotic events such as pulmonary embolism.¹ Although, presence of free floating right heart thrombus is unusual situation in patients with massive pulmonary embolism.

A 56-year-old caucasian male with morbid obesity (BMI 45 kg/m²), with 15-day history of dyspnea, myalgia and dry cough, was admitted to emergency room. First rapid SARS-CoV-2 PCR was negative, but with high clinical suspicion, pharmacological treatment was started. Tachypnea and dry crackles were observed at physical examination. Laboratories studies showed white-cell count $15.80 \times 10^9/L$ (12% lymphocytes), lactate dehydrogenase 425 U/L, C-reactive protein 3.82 mg/dl and D-dimer 32,000 mcg/L. Arterial blood gas PaO₂ 55 mmHg at room air. CT pulmonary angiography (CTPA) could not be performed due to patient's anthropometry. According to high probability of pulmonary embolism (PE), a transthoracic echocardiogram was practiced, revealing multiple thrombus at the right atrium and right ventricle, severe dilatation of the right cavities with signs of overload right ventricle and significant PAH (pulmonary arterial pressure 110 mmHg). Low molecular weight heparin was initiated. Despite negative PCR results, up to three SARS-CoV-2 PCR kept negative results. After a significant weight loss, CTPA could be performed showing filling defects in the main pulmonary artery consistent with pulmonary embolism and ground-glass areas in both upper lobes and left lower lobe. Patient rest instable with severe respiratory failure, subsequently thrombolysis with reteplase was performed with good outcomes. Echocardiogram after procedure showed the absence of intracardiac thrombus and reduced PAH (60 mmHg). Even though having three negative rapid SARS-CoV-2 PCR, 10 days later, serologies showed positive results for IgG (Elisa technique), which confirmed Covid-19 pulmonary affection diagnosis.

SARS-CoV-2 infection generates coagulation disorders with elevated D-dimer values, due to systemic pro-inflammatory cytokine to activate procoagulant factors, which predispose to thromboembolic events like PE.²

Obesity (BMI > 35 kg/m²) is widely reported as a risk factor for thromboembolic disease (especially pulmonary embolism and deep venous thrombosis). Thromboembolic mechanisms generated in morbid obesity include increased platelet activity, procoagulant states, altered fibrinolysis, and endothelial cell activation.³

Dyspnea, as a prevailing symptom of COVID19 pneumonia, makes clinical recognition of PE quite challenging, therefore diagnostics tests are needed for rapid management, and imaging techniques such CT pulmonary angiography are conveniently. In patients with PE, the existence of intracardiac thrombosis in right cardiac cavities is unusual unless atrial fibrillation is set, occurring between 4 and 18% in cases of massive PE. Combination of massive PE an intracardiac thrombosis it's a medical emergency with increased mortality, which requires an urgent treatment. Thrombolysis is usually the best choice due to the double target of the therapy, the PE and the cardiac thrombus.⁴

The diagnostic challenge that arises is that, even with the clinical suspicion of COVID19 infection, with acute respiratory failure and massive PE with intracardiac thrombosis, needing urgent diagnosis and treatment, plus a negative result of a PCR test cannot stop the attitude and management to follow up. The Real-Time reverse-transcriptase polymerase chain reaction (RT-PCR) can present false negatives due to the low viral charge obtained in the sample, requiring the detection of antibodies for the diagnostic. Jin et al. show a sensitivity higher than 90% in IgM and IgG test compared to molecular detection, after 5 days since the realization of serological tests.⁵

In conclusion, although obesity is an independent risk factor for thromboembolic events, other factors must be considered, especially coagulation disorders caused by COVID19 infection. Then, the presence of negative PCR for SARS-CoV-2 healthcare providers should not neglect the disease, so a subsequent serological study may confirm the diagnosis.

Conflicts of interest

Authors declare no conflicts of interest.

References

- Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1 MERS-CoV and lessons from the past. *J Clin Virol*. 2020;127:104362. <http://dx.doi.org/10.1016/j.jcv.2020.104362>.
- Han H, Yang L, Liu R, Liu F, Wu KL, Li J, et al. Prominent changes in blood-coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med*. 2020. <http://dx.doi.org/10.1515/cclm-2020-0188>.
- Faber DR, de Groot PG, Visseren FL. Role of adipose tissue in haemostasis, coagulation and fibrinolysis. *Obes Rev*. 2009;10:554–63. <http://dx.doi.org/10.1111/j.1467-789X.2009.00593.x>.
- Charif F, Mansour MJ, Hamdan R, Najjar C, Nassar P, Issa M, et al. Free-floating right heart thrombus with acute massive pulmonary embolism: a case report and review of the literature. *J Cardiovasc Echogr*. 2018;146–9. <http://dx.doi.org/10.4103/jcecho.jcecho.64.17>.
- Jin Y, Wang M, Zuo Z, Fan C, Ye F, Cai Z, et al. Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019. *Int J Infect Dis*. 2020;94:49–52. <http://dx.doi.org/10.1016/j.ijid.2020.03.065>.

Jordi Juanola Pla^{a,b,*}, Berta Ferreiro Rodriguez^c, Concepció Falga Tirado^d